

Abstract No. niko288

Structural Studies of Eph Receptor Tyrosine Kinases and Ephrins

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Beamline(s): X9A

ABSTRACT: Eph receptors represent the largest subfamily of receptor tyrosine kinases (RTKs). The Eph RTKs and their ligands, the ephrins, play important roles during the formation of many different embryonic boundaries. They are predominantly expressed in the developing and adult nervous system, where they are involved in contact-mediated axon guidance, axon fasciculation, and cell migration. Understanding Eph signaling is, therefore, essential for development of methods for treatment of brain and spinal cord injuries. In addition, the Eph RTKs and ephrins play an important role in angiogenesis and vasculogenesis, which defines them as potential targets for anti-cancer drugs. Eph receptors are unique among other RTKs in that they fall into two subclasses with distinct ligand specificities, and in that they can also function as ligands activating bi-directional signaling. Two years ago we determined the crystal structure of the ligand-binding domain of EphB2 using the Multiple Isomorphous Replacement (MIR) method. Now, we have obtained crystals of the EphB2-ephrinB2 complex. These crystals belonged to the C2 space group and diffract to 3.0 Å at beamline X9A at NSLS. We collected a native and several derivative data sets. We have also obtained a new crystal form, which grows only with Se-methionine modified EphB2. These P1 crystals are much less mosaic and diffract to a slightly higher resolution. Structure determination is underway.